22. "Introduction to Tissue Engineering: A Glimpse into the Future," American Society of Plastic Surgeons Annual Scientific Meeting, San Antonio, Texas, November 4, 2002.
23. "Cell-Based Therapies and Tissue Engineering," Sponsored by Case Western Reserve University, Cleveland, Ohio, May 27-31, 2003.
24. "Advances in Tissue Engineering," Sponsored by Rice University, Houston, Texas, August 13-16, 2003.
25. "Current Progress in Tissue Engineering," Sponsored by Harvard Medical School, Boston, Massachusetts, October 2-3, 2003.
26. "Cell-Based Therapies and Tissue Engineering," Sponsored by Case Western Reserve University, Cleveland, Ohio, May 17-21, 2004.
27. "Summer School on Emerging Technologies in Biomedicine," Sponsored by the University of Patras, Patras, Greece, June 20-25, 2004.
28. "Advances in Tissue Engineering," Sponsored by Rice University, Houston, Texas, August 11-14, 2004.
29. "Cell-Based Therapies and Tissue Engineering," Sponsored by Case Western Reserve University, Cleveland, Ohio, May 31-June 3, 2005.
30. "Advances in Tissue Engineering," Sponsored by Rice University, Houston, Texas, August 10-13, 2005.
31. "Cell-Based Therapies and Tissue Engineering," Sponsored by Case Western Reserve University, Cleveland, Ohio, May 22-26, 2006.
32. "Advances in Tissue Engineering," Sponsored by Rice University, Houston, Texas, August 16-19, 2006.
33. "Cell-Based Therapies and Tissue Engineering," Sponsored by Case Western Reserve University, Cleveland, Ohio, May 21-25, 2007.
34. "Advances in Tissue Engineering," Sponsored by Rice University, Houston, Texas, August 15-18, 2007.
35. "Cell-Based Therapies and Tissue Engineering," Sponsored by Case Western Reserve University, Cleveland, Ohio, May 19-23, 2008.
36. "Advances in Tissue Engineering," Sponsored by Rice University, Houston, Texas, August 13-16, 2008.

Research Grants (Total Costs)

Principal Investigator

1. T.N. Law Professorship in Bioengineering (1992-96)
   $ 150,000

2. Rice University - Biomedical Research Support Grant (1992-93)
   "Tissue Engineering by Cell Transplantation"
   $ 4,800

3. National Science Foundation - Research Equipment Grant (1992-93)
   "Gel Permeation Chromatography System for Bioengineering Research"
   $ 26,567 (with Drs. J.V. Shanks and K. Zygourakis)

4. Rice University - Biomedical Research Support Grant (1992-93)
"UV/VIS System for Research in Biosciences and Bioengineering"
$ 3,100 (with Drs. J.V. Shanks and K. Zygourakis)

5. Orthopedic Research and Education Foundation (1993-95)
"A Temporary Replacement for Trabecular Bone: Biodegradable Particulate Composites with Osteoblast Transplantation for Orthopaedic Applications"
$ 97,277 (with Dr. M.J. Yaszemski)

6. Texas Biotechnology Corporation, Houston, Texas (1993-95)
"Bioresorbable Polymer Delivery of Antisense Oligonucleotides"
$ 53,068

7. American Cyanamid Company, Princeton, New Jersey (1994-95)
"Controlled Release Systems for Bioactive Macromolecules"
$ 5,000

8. The Whitaker Foundation (1994-97)
"Polymeric Delivery Systems for Antisense Oligonucleotides"
$ 179,617

9. Johnson&Johnson Medical (1994-95)
"Biodegradable Polymer Foams for Dermal Tissue Repair"
$ 18,834

10. C.A. Garcia Fund for Eye Research (1995-96)
"Retinal Pigment Epithelium Regeneration"
$ 19,503

11. National Retinitis Pigmentosa Foundation (1995-98)
"Mechanical and Immunological Phenomena Affecting Survival of Transplanted Retinal Pigment Epithelial Cells"
$ 113,208 (with Drs. D. Lahiri-Munir and C.A. Garcia)

12. National Aeronautics and Space Administration (1996-2001)
"Mechanical Load Effects on Bone Formation"
$ 424,690 (with Dr. P. Whitson)

13. National Institutes of Health - FIRST Award (1996-2001)
"Bone Regeneration by Osteoblast Transplantation"
$ 523,250

14. National Aeronautics and Space Administration (1996-97)
"Analysis of Mechanical Loading Effects on Bone Formation and Remodeling"
$ 22,000

15. National Institutes of Health (1996-2001)
"Injectable Biomaterials for Bone Tissue Engineering"
$ 729,637

16. Defense Advanced Research Projects Agency (1997-99)
"Biomimetic Materials for Pathogen Neutralization"
$ 779,612

17. National Institutes of Health (1998-2003)
"*In Situ* Polymerizable Gels for Dental Tissue Engineering"
$ 1,379,306

18. Chrysalis BioTechnology, Galveston, Texas (1998-99)
"Microparticle Biodegradable Polymeric Delivery Systems for Bioactive Molecules"
$ 17,940

19. Molecular Geodesics, Boston, Massachusetts (1999-2000)
"Biomimetic Materials for Pathogen Neutralization"
$ 12,400

20. National Institutes of Health (1999-2004)
"Strength and Resorption of Biodegradable Skull Implants"
$ 511,435

21. Toray Industries, Shiga, Japan (2000-02)
"Development of Biocompatible Materials"
$ 20,000

22. Chrysalis BioTechnology, Galveston, Texas (2001-02)
"Controlled Release Systems for Bioactive Molecules"
$ 30,000

23. Desmogen, Bellaire, Texas (2001-02)
"Biomaterials Development for Vertebroplasty"
$ 100,000

24. National Science Foundation (2001-06)
"Nanocomposites for Bone Replacement"
$ 260,980

25. Advanced Technology Program of the State of Texas (2002-03)
"Novel Scaffold Design and Evaluation Technique for Engineering Bone Replacement Tissue"
$ 187,500 (with Dr. M.A.K. Liebschner)

26. National Institutes of Health (2002-07)

"Bone Regeneration by Osteoblast Transplantation"
$ 1,163,237

27. Bausch & Lomb, Rochester, New York (2002-03)
"Injectable Ocular Drug Delivery Systems"
$ 100,053

28. National Institutes of Health (2003-08)
"Injectable Cellular Composites for Cartilage Engineering"
$ 1,681,524

29. Bausch & Lomb, Rochester, New York (2003-04)
"Injectable Ocular Drug Delivery Systems"
$ 100,000

30. National Institutes of Health (2004-09)
"Promotion of Alveolar Socket Healing with Biopolymers"
$ 1,528,360

31. Bausch & Lomb, Rochester, New York (2004-05)
"Ocular Drug Delivery Systems"
$ 100,000

32. National Institutes of Health (2005-10)
"Tissue Engineering of Hematopoietic Bone"
$ 240,503

33. Bausch & Lomb, Rochester, New York (2005)
"Ocular Drug Delivery Systems"
$ 30,000

34. Dan L. Duncan Cancer Center, Houston, Texas (2006-07)
"Maintenance of Ovarian Reserve after Cancer Chemotherapy"
$ 80,000

35. Rice University - International Collaboration Travel Fund (2007)
"Global Approaches in Tissue Engineering"
$ 9,800

36. National Institutes of Health (2008-13)
"*In Situ* Hardening Cellular Constructs for Craniofacial Bone Regeneration"
$ 1,648,295

37. Department of Defense (2008-13)
"Antibiotic Releasing Space Maintainer and Prefabricated Vascularized Bone Flap"
$ 1,998,009

38. Rice University - International Collaboration Travel Fund (2008)
"Manufacturing and Scale-Up Towards Clinical Treatments of Craniofacial Trauma: A Collaborative Effort Between Rice University and the National Tissue Engineering Center of China"
$ 7,000

39. SpinalCyte, Houston, Texas (2008-2010)
"Repair of Cartilage Using an *In Vitro* Bioreactor"
$ 300,000

40. Celthera, Hopkinton, Massachusetts (2008-2009)
"Bone Regeneration Using Scaffold-Reinforced Hydrogel/Whole Marrow Constructs"
$ 65,000

41. National Institutes of Health (2008-10)
"Regulated Osteochondrogenesis of Human Mesenchymal Stem Cells Using Gene Delivery"
$ 360,272

42. Defense Advanced Research Projects Agency (2008-10)
"BioNanoScaffolds (BNS) for Post-Traumatic Osteoregeneration"
$ 1,200,000

Co-Principal Investigator

1. The Whitaker Foundation - Biomedical Engineering Special Opportunity Award (1995-98)
"Frontiers in Cellular and Tissue Engineering"
$ 750,000 (Dr. L.V. McIntire, P.I.)

2. National Science Foundation (1995-98)
"Light Scattering Detector for Polymer Research"
$ 20,600 (Part of "Radical Reactions of the Azo and Azoxy Groups," $ 406,000, Dr. P.S. Engel, P.I.)

3. University of Texas M.D. Anderson Cancer Center - Physicians Referral Service (1995-96)
"Tissue Engineered Bone Flaps in Sheep"
$ 31,295 (Dr. M.J. Miller, P.I.)

4. University of Texas M.D. Anderson Cancer Center - Physicians Referral Service (1995-96)
"*In Vivo* Evaluation of Recombinant Human Bone Morphogenetic Protein-2 as a Bone Graft Substitute for Cavitary Bone Defects"
$ 43,170 (Dr. A.W. Yasko, P.I.)

5. The Whitaker Foundation - Biomedical Engineering Development Award (1996-2001)
"New Frontiers in Biomedical Engineering Education and Research"

$ 5,000,000 (Dr. L.V. McIntire, P.I.)

6. Department of Defense (1996-97)
"Solid State NMR for the Characterization of Functional Materials"
$ 200,000 (Dr. A.R. Barron, P.I.)

7. The Whitaker Foundation - Biomedical Engineering Leadership Award (1998-2003)
$ 6,000,000 (Dr. L.V. McIntire, P.I.)

8. National Institutes of Health - Biotechnology Research Training Grant (2001-06)
$ 1,506,761 (Dr. L.V. McIntire, P.I.)

9. National Science Foundation - Integrative Graduate Education and Research Training Grant in Cellular Engineering (2001-06)
$ 2,620,649 (Dr. L.V. McIntire, P.I.)

10. National Science Foundation – Nanoscale Science and Engineering Center (2001-06)
"Center for Nanoscience in Biological and Environmental Engineering"
$ 10,539,998 (Dr. R.E. Smalley, P.I.)

Students Supervised

Postdoctoral Research

Rice University:
Markus S. Widmer, Ph.D. (ETH Zürich, 1995), 1995-1997
Julia E. Babensee, Ph.D. (University of Toronto, 1996), 1996-1999
Raman V. Bahulekar, Ph.D. (University of Poona, 1991), 1997-1999
Aaron S. Goldstein, Ph.D. (Carnegie Mellon University, 1997), 1997-1999
Guizhen Liu, M.D. (University of Zürich, 1993), 1997-1999
Qing Liu, Ph.D. (Leiden University, 1997), 1997-1999
Zewen Liu, Ph.D. (University of Tulane, 1996), 1997-1998
Guoming Zhu, M.D. (Shanghai Medical University, 1985), 1997-1998
Shulin He, Ph.D. (University of Gent, 1993), 1998-1999
Seongbong Jo, Ph.D. (Purdue University, 1998), 1998-2000, 2002-2003
Georgios Stamatas, Ph.D. (Rice University, 1998), 1998
Lichun Lu, Ph.D. (Rice University, 1999), 1999-2000
William T. Godbey, Ph.D. (Rice University, 1999), 1999-2000
Vassilios I. Sikavitsas, Ph.D. (State University of New York at Buffalo, 1999), 1999-2002
Joerg Tessmar, Ph.D. (University of Regensburg, 2002), 2002-2004
German Research Foundation Postdoctoral Fellowship, 2002-2004
Hiroki Ueda, Ph.D. (Kyoto University, 2001), 2003-2004
Japanese Science Foundation Postdoctoral Fellowship, 2003-2004
Johnna S. Temenoff, Ph.D. (Rice University, 2003), 2003-2005
National Institutes of Health Craniofacial-Oral Biology Program Trainee, 2004-2005
Michael C. Hacker, Ph.D. (University of Regensburg, 2004), 2004-2007

German Research Foundation Postdoctoral Fellowship, 2005-2007

Upma Sharma, Ph.D. (Princeton University, 2005), 2005-2006

First Prize, Keck Center Annual Research Conference Poster Contest, Gulf Coast Consortia, 2005

National Institutes of Health Nanobiology Program Trainee, 2005-2006

Elizabeth Christenson, Ph.D. (Case Western Reserve University, 2005), 2005-2007

National Institutes of Health Craniofacial-Oral Biology Program Trainee, 2005-2007

Mark Sweigart, Ph.D. (Rice University, 2005), 2005-2006

F. Kurtis Kasper, Ph.D. (Rice University, 2005), 2005-2008

National Institutes of Health Nanobiology Program Trainee, 2007-2008

Balaji Sitharaman, Ph.D. (Rice University, 2005), 2005-2007

Center for Nanoscale Science and Technology Evans Atwell Fellowship, 2005-2007

Theoni K. Georgiou, Ph.D. (University of Cyprus, 2006), 2006-2007

Meng Shi, Ph.D. (University of Toronto, 2008), 2008-present

Milind Singh, Ph.D. (University of Kansas, 2008), 2008-present

Graduate Research

Rice University:

Susan L. Ishaug-Riley, Ph.D., 1992-1996

Graduate Student Award for Outstanding Research, Society For Biomaterials, 1997

Ralph Budd Award for Best Engineering Ph.D. Thesis, Rice University, 1997

Ph.D. Thesis Award: Runner Up, Sigma Xi, Rice University/Texas Medical Center, 1997

Dr. William B. Walsh Award for Excellence in Bioengineering, Advanced Tissue Sciences, 1996

First Prize, Chemical Engineering Graduate Research Symposium, Rice University, 1996

First Prize, Chemical Engineering Graduate Research Poster Contest, Rice University, 1996

Poster Award: Honorable Mention, Houston Society for Engineering in Medicine and Biology, 1996

Second Prize, Chemical Engineering Graduate Research Symposium, Rice University, 1995

Robert C. Thomson, Ph.D., 1992-1997

Robert L. Cleek, Ph.D., 1993-1997

Selected Excellence Paper, Society For Biomaterials, 1997

Intermedics Best Poster Award, Houston Society for Engineering in Medicine and Biology, 1995

Anna C. Jen, M.S., 1993-1997

NASA Graduate Student Researchers Program Trainee, 1996-1997

National Institutes of Health Biotechnology Program Trainee, 1994-1996

Laura J. Suggs, Ph.D., 1993-1998

Excellence in Science Dissertation Award for Best Ph.D. Thesis, Sigma Xi, Rice University/ Texas Medical Center, 1998

Graduate Student Award for Best Paper, Southern Biomedical Engineering Conference, 1998

Hershel M. Rich Invention Award, Rice University, 1997

National Institutes of Health Biotechnology Program Trainee, 1995-1997

M. Conley Wake, M.S., 1993-1997

Lodieska Stockbridge Vaughan Fellowship, Rice University, 1996

Third Prize, Chemical Engineering Graduate Research Symposium, Rice University, 1996

Distinguished Contribution, BFGoodrich Collegiate Inventors Program, 1995

National Science Foundation Graduate Fellowship, 1993-1996

Lichun Lu, Ph.D., 1994-1999

Susan J. Peter, Ph.D., 1994-1998

Graduate Student Award for Outstanding Research, Society For Biomaterials, 1998

Graduate Student Award Finalist, Materials Research Society Spring Meeting, 1998

National Institutes of Health Biotechnology Program Trainee, 1996-1998

Richard G. Payne, Ph.D., 1995-2001

Ralph Budd Award for Best Engineering Ph.D. Thesis, Rice University, 2002

First Prize, Chemical Engineering Graduate Research Poster Contest, Rice University, 1999

National Institutes of Health Biotechnology Program Trainee, 1997-1999

Hershel M. Rich Invention Award, Rice University, 1997

Hershel M. Rich Invention Award, Rice University, 1995

Esfandiar Behravesh, Ph.D., 1997-2002

William T. Godbey, Ph.D., 1997-1999

Graduate/Postdoc Award on Innovative Aspects of Controlled Drug Release, Controlled Release Society-Capsugel, 2000

National Science Foundation Graduate Fellowship, 1997-1999

Albert K. Shung, M.S., 1997-2002

Gregory N. Bancroft, Ph.D., 1998-2002

Best Poster Award, Baylor College of Medicine M.D./Ph.D. Symposium, 2001

Best Paper Award, Texas Medical Scientist Training Program Conference, 2000

Transco Scholarship, 1998-2002

John P. Fisher, Ph.D., 1998-2002

National Science Foundation Center for Biological and Environmental Nanotechnology Trainee, 2001-2003

Best Poster Award, Materials Research Society Fall Meeting, 2000

Jeremy S. Blum, Ph.D., 1998-2003

National Science Foundation Integrative Graduate Education and Research Program Trainee, 2001-2003

Heungsoo Shin, Ph.D., 1998-2003

Graduate Student Award for Outstanding Research, Society For Biomaterials, 2002

Johnna S. Temenoff, Ph.D., 1998-2003

Ralph Budd Award for Best Engineering Ph.D. Thesis, Rice University, 2004

Whitaker Foundation Graduate Fellowship, 1998-2003

Mark D. Timmer, Ph.D., 1998-2003

National Science and Engineering Research Council Fellowship, 2000-2003

National Institutes of Health Biotechnology Program Trainee, 1999-2000

Jeffrey E.-K. Chen, M.S., 1999-2002

Elizabeth L. Hedberg, Ph.D., 1998-2004

National Science Foundation Center for Biological and Environmental Nanotechnology Trainee, 2003-2004
Tissue Engineering Special Interest Group Student Award, Society For Biomaterials, 2002
National Institutes of Health Biotechnology Program Trainee, 2001-2002
National Institutes of Health Biotechnology Program Trainee, 1999-2000

Heidi L. Holtorf, Ph.D., 1999-2004
Graduate Student Award for Outstanding Research, Society For Biomaterials, 2005
National Science Foundation Integrative Graduate Education and Research Program Trainee, 2001-2003

F. Kurtis Kasper, Ph.D., 1999-2005
Sallyport Award, Association of Rice Alumni, 2006
National Science Foundation Integrative Graduate Education and Research Program Trainee, 2001-2003

Manuela E. Gomes, Ph.D., 2001-2004
Portuguese Foundation for Science and Technology Graduate Fellowship, 2001-2004

Theresa A. Holland, Ph.D., 2001-2005
Whitaker Foundation Graduate Fellowship, 2001-2005

Amit S. Mistry, Ph.D., 2002-2007
First Prize, National Institutes of Health Biotechnology Graduate Training Program Poster Contest, Rice University, 2004
National Institutes of Health Biotechnology Program Trainee, 2003-2005

Zarana S. Patel, Ph.D., 2002-2007
National Science Foundation Graduate Fellowship, 2003-2006

Xinfeng Shi, Ph.D., 2002-2007
Poster Award: Runner Up, Houston Society for Engineering in Medicine and Biology, 2004
First Prize, Bioengineering Graduate Research Poster Contest, Rice University, 2004

Hansoo Park, Ph.D., 2003-2007

Sheila A. Moore, M.S., 2003-2007

Matthew B. Murphy, Ph.D., 2003-2008
National Science Foundation Integrative Graduate Education and Research Program Trainee, 2005-2006

Quynh P. Pham, Ph.D., 2003-2007

Simon Young, Ph.D., 2003-2008
Oral Abstract Scientific Presentation Award, Annual Meeting of the American Association of Oral and Maxillofacial Surgeons, 2007
Oral and Maxillofacial Surgery Foundation Research Fellowship, 2004-2006

Sue Anne Chew, Ph.D. Candidate, 2004-present

Xuan Guo, Ph.D. Candidate, 2004-present

Jiehong Liao, Ph.D. Candidate, 2004-present

Anita Saraf, Ph.D. Candidate, 2004-present
National Science Foundation Integrative Graduate Education and Research Program Trainee, 2005-2006

Leda Klouda, Ph.D. Candidate, 2005-present
Edgar O'Rear Travel Grant, Institute of Biosciences and Bioengineering, Rice University, 2007

Gerondelis Foundation Scholarship, 2007
James D. Kretlow, Ph.D. Candidate, 2005-present
National Institutes of Health Biotechnology Program Trainee, 2006-2008
National Institutes of Health Nanobiology Program Trainee, 2008-present
Andrea Haesslein, M.S., 2006-2007
Richard A. Thibault, Ph.D. Candidate, 2006-present
Ruth L. Kirschstein National Research Service Award, National Institutes of Health, 2008-present
Travel Award, 3rd Aegean Conference on Tissue Engineering, Rhodes, Greece, 2008
Emily L. Burdett, Ph.D. Candidate, 2007-present
National Institutes of Health Biotechnology Program Trainee, 2008-present
Paschalia M. Mountziaris, Ph.D. Candidate, 2007-present
National Institutes of Health Nanobiology Program Trainee, 2008-present

M.I.T.:
Heidi L. Wald, M.S., 1990-1991

Undergraduate Research

Rice University:
M. Conley Wake, 1992-1993
National Science Foundation Graduate Fellowship, 1993
POLYED Award for Outstanding Undergraduate Polymer Research, American Chemical Society, 1993
James S. Waters Creativity Award, Rice University, 1993
Marta A. West, 1992-1993
Undergraduate Scholar Award, Rice University, 1993
Horst A. von Recum, 1993
Matthew D. Allen, 1994-1995
Christine M. Bardsley, 1994
Joel H. Collier, 1994
Susan A. Hoffman, 1994
David Jaber, 1994
Keith Johnson, 1994
Julie L. Morris, 1994-1995
Terri A. Shefelbine, 1994
National Science Foundation Graduate Fellowship, 1995
Coy R. Stine, 1994
Alyssa R. Terk, 1994, 1996
Genevieve M. Crane, 1995-1996
Marshall Fellowship, 1996
National Science Foundation Graduate Fellowship, 1996
Whitaker Foundation Graduate Fellowship, 1996
James S. Waters Creativity Award, Rice University, 1996
John P. McGovern Outstanding Pre-Medical Student Award, Rice University, 1996

First Prize, The Institute of Biosciences and Bioengineering / Biochemistry and Cell Biology Poster Retreat (Undergraduate Seniors Category), Rice University, 1996
POLYED Award for Outstanding Undergraduate Polymer Research, American Chemical Society, 1995

Cameron A. Etezadi, 1995-1996
Puneet K. Gupta, 1995-1997
Travis W. Hopp, 1995-1997
Edmund Y.-C. Kao, 1995-1996
National Science Foundation Graduate Fellowship, 1996
Joyce L. Almaguer, 1996-1997
S. David Cho, 1996-1997
C. Alejandra Garcia, 1996-1998
Daniel J. Kim, 1996-1998
James S. Waters Creativity Award, Rice University, 1997
Poster Award: Runner Up, Houston Society for Engineering in Medicine and Biology, 1997
Ravi S. Krishnan, 1996-1997
Valerie A.-L. Liu, 1996-1998
National Science Foundation Graduate Fellowship, 1998
Whitaker Foundation Graduate Fellowship, 1998
Jessica A. Nolley, 1996
Fulbright Fellowship, 1997
Saumya A. Sivaram, 1996-1999
Karen C. Ting, 1996
Paul Kim, 1997-1998
Catalina R. Liang, 1997-1998
Laurie L. Palombo, 1997
Angela S.-Y. Peng, 1997-1998
Charlos C. Ward, 1997
Kimathi S.R. Blackwood, 1998
Sheila A. Herman, 1998-1999
Special Award for Originality, Annual Biosciences Undergraduate Poster Session, 1999
Tiffany M. Juarez, 1998-2000
Grayson E. Morris, 1998
National Science Foundation Graduate Fellowship, 1999
Kavita Nyalakonda, 1998-1999
Joseph S. McGonigle, 1999-2000
Mehul N. Tejani, 1999
Weera Chainakul, 2000
Theresa A. Holland, 2000-2001
National Science Foundation Graduate Fellowship, 2001
Whitaker Foundation Graduate Fellowship, 2001
National Defense Science and Engineering Fellowship, 2001
James S. Waters Creativity Award, Rice University, 2001
Best Poster Award, Materials Research Society Fall Meeting, 2000
George R. Brown Undergraduate Research Intern, Rice University, 2000

Jerzy Rokicki, 2000-2002
Century Scholar, 2000-2002
Robert W. Schroeter, 2000
R. Adam Horch, 2001-2004
National Science Foundation Center for Biological and Environmental Nanotechnology Trainee, 2002-2004
Century Scholar, 2001-2003
Charles K.-J. Shih, 2001-2004
George R. Brown Undergraduate Research Intern, Rice University, 2002-2003
National Science Foundation Center for Biological and Environmental Nanotechnology Trainee, 2001-2002
Emily S. Steinbis, 2001-2002
Second Prize, Rice Undergraduate Research Symposium, Rice University, 2002
John W. Baker, 2002
Carla M. Bossano, 2002-2003
Beth M. Boulden, 2002
Marc A. Burrell, 2002-2004
Century Scholar, 2002-2004
Daniel E. Conway, 2002-2003
National Science Foundation Graduate Fellowship, 2003
Néha Datta, 2002-2006
Distinguished Senior Award, Rice Engineering Alumni Association, 2006
Outstanding Contributions to Research Bioengineering Award, Rice University, 2006
James S. Waters Creativity Award, Rice University, 2004
Century Scholar, 2002-2004
Julia L. Pergola, 2002-2003
George R. Brown Undergraduate Research Intern, Rice University, 2003
Stephanie K. Seidlits, 2002-2003
Todd T. Tomson, 2002
Geng Chen, 2003-2004
Century Scholar, 2003-2004
Cara R. Rieger, 2003-2004
Timothy Borden, 2004-2006
Century Scholar, 2004-2006
Eric Huang, 2004-2005
Century Scholar, 2004-2005
Erin D. Jerkins, 2004-2005
Patrick P. Spicer, 2004-2006
Tommy Fu, 2005-2007
Century Scholar, 2005-2007
Supriya Hattangadi, 2005-2007
Century Scholar, 2005-2007
Brandy Ma, 2005-2006
Julie M. Mani, 2005-2006
Salman A. Rahman, 2005-2007
Marina N. Boleda, 2006-2007

Stacy H. Cheng, 2006-2007
Roxana R. Daneshjou, 2006-
Century Scholar, 2006-
Jennifer L. Holm, 2006-2007
Wafa Soofi, 2006-2007
Katherine L. Wu, 2006-2007
Tiffany Yeh, 2006-2007
Tiffany J. Siu, 2007
Laura H. Barg-Walkow, 2007-
Century Scholar, 2007-
Brian T. Benjamin, 2007-
Diane Chen, 2007-
Century Scholar, 2007-
Genevieve Lozier, 2007-

M.I.T.:
Amy J. Thorsen, 1990
Yuan Bao, 1990-1991
Lisa A. Czerwonka, 1990-1991
Hui-Lin Lai, 1990-1991
Georgios Sarakinos, 1990-1991
Amy M. Whiteman, 1990-1991
Joseph F. Cotten, 1991
Susan M. Leite, 1991

Purdue University:
Lyn M. Eshelman, 1986
Candace J. Chang, 1987
Daphne M. Williams, 1987

Ph.D. Theses Supervised

1. Susan L. Ishaug-Riley, "Bone Formation by Three-Dimensional Osteoblast Culture in Biodegradable Poly(α-Hydroxy Ester) Scaffolds," Ph.D. Thesis, Department of Chemical Engineering, Rice University, June 1996.
2. Robert C. Thomson, "Biodegradable Polymer Scaffold Fabrication and the Creation of Tissue Engineered Bone," Ph.D. Thesis, Department of Chemical Engineering, Rice University, April 1997.
3. Robert L. Cleek, "Polymeric Delivery of Inhibitors of Smooth Muscle Cell Proliferation," Ph.D. Thesis, Department of Chemical Engineering, Rice University, May 1997.
4. Susan J. Peter, "Injectable, *In Situ* Polymerizable, Biodegradable Scaffolds Based on Poly(Propylene Fumarate) for Guided Bone Regeneration," Ph.D. Thesis, Department of Chemical Engineering, Rice University, May 1998.
5. Laura J. Suggs, "Development of Poly(Propylene Fumarate-co-Ethylene Glycol): An Injectable, Biodegradable Implant for Cardiovascular Applications," Ph.D. Thesis, Department of Chemical Engineering, Rice University, May 1998.

6. Lichun Lu, "Modulation of Cell Morphology and Function Using Synthetic Biodegradable Polymers," Ph.D. Thesis, Department of Chemical Engineering, Rice University, May 1999.
7. William T. Godbey, "Poly(Ethylenimine) as a Gene Delivery Vehicle, and Its Potential for Gene Therapy," Ph.D. Thesis, Department of Biochemistry and Cell Biology, Rice University, August 1999.
8. Richard G. Payne, "Development of an Injectable, *In Situ* Crosslinkable, Degradable Polymeric Carrier for Osteogenic Populations," Ph.D. Thesis, Department of Chemical Engineering, Rice University, October 2001.
9. Gregory N. Bancroft, "Bone Tissue Engineering by Cell and Matrix Transplantation," Ph.D. Thesis, Department of Bioengineering, Rice University, May 2002.
10. Esfandiar Behravesh, "Synthesis of an Injectable Biodegradable Biomimetic Macroporous Hydrogel Scaffold for Bone Tissue Engineering," Ph.D. Thesis, Department of Bioengineering, Rice University, August 2002.
11. John P. Fisher, "The Development of a Photocrosslinked Biomaterial for Bone Tissue Engineering Applications," Ph.D. Thesis, Department of Bioengineering, Rice University, October 2002.
12. Mark D. Timmer, "Development of a Biodegradable Interbody Fusion Device," Ph.D. Thesis, Department of Bioengineering, Rice University, July 2003.
13. Heungsoo Shin, "Development of Biodegradable, Biomimetic Hydrogels Modulating Cellular Function for Guided Bone Regeneration," Ph.D. Thesis, Department of Bioengineering, Rice University, August 2003.
14. Johnna S. Temenoff, "Development of Thermally-Crosslinked Hydrogels as Injectable Cell Carriers for Orthopaedic Tissue Engineering," Ph.D. Thesis, Department of Bioengineering, Rice University, August 2003.
15. Jeremy S. Blum, "Development of Genetically Modified Cells for Bone Tissue Regeneration," Ph.D. Thesis, Department of Bioengineering, Rice University, October 2003.
16. Elizabeth L. Hedberg, "Controlled Release of Osteogenic Factors from Injectable Biodegradable Composite Materials for Bone Tissue Engineering," Ph.D. Thesis, Department of Bioengineering, Rice University, April 2004.
17. Manuela E. Gomes, "A Bone Tissue Engineering Strategy Based on Starch Scaffolds and Bone Marrow Cells Cultured in a Flow Perfusion Bioreactor," Department of Polymer Engineering, University of Minho, Portugal, October 2004.
18. Heidi L. Holtorf, "Modulation of Marrow Stromal Cell Differentiation in Bone Tissue Engineering Constructs," Ph.D. Thesis, Department of Bioengineering, Rice University, December 2004.
19. F. Kurtis Kasper, "Investigation of Oligo(Poly(Ethylene Glycol) Fumarate) Hydrogels for Controlled Release of Plasmid DNA," Ph.D. Thesis, Department of Bioengineering, Rice University, September 2005.
20. Theresa A. Holland, "Controlled Growth Factor Delivery from Biodegradable Hydrogel Scaffolds for Articular Cartilage Repair," Ph.D. Thesis, Department of Bioengineering, Rice University, December 2005.
21. Xinfeng Shi, "Development of Injectable Nanocomposite Scaffolds of Single-Walled Carbon Nanotubes and Biodegradable Polymers for Bone Tissue Engineering," Ph.D. Thesis, Department of Bioengineering, Rice University, February 2007.

22. Hansoo Park, "Injectable Cell/Hydrogel Composites for Articular Cartilage Tissue Engineering," Ph.D. Thesis, Department of Bioengineering, Rice University, April 2007.
23. Amit S. Mistry, "Degradation and Biocompatibility of a Fumarate-Based/Alumoxane Nanocomposite for Bone Tissue Engineering," Ph.D. Thesis, Department of Bioengineering, Rice University, April 2007.
24. Zarana S. Patel, "Controlled Delivery of Angiogenic and Osteogenic Growth Factors for Bone Regeneration," Ph.D. Thesis, Department of Bioengineering, Rice University, August 2007.
25. Quynh P. Pham, "Modulation of the Osteoblastic Differentiation of Marrow Stromal Cells for Bone Tissue Engineering," Ph.D. Thesis, Department of Bioengineering, Rice University, December 2007.
26. Simon Young, "The Effect of Simultaneous, Controlled Release of Angiogenic and Osteogenic Growth Factors on the Enhancement of Osteogenesis within Craniofacial Defects," Ph.D. Thesis, Department of Bioengineering, Rice University, May 2008.
27. Matthew B. Murphy, "Targeted Delivery of Osteogenic Drugs for Bone Tissue Engineering," Ph.D. Thesis, Department of Bioengineering, Rice University, May 2008.

M.S. Theses Supervised

1. M. Conley Wake, "Fabrication of Pliable Polymer Scaffolds for Tissue Engineering and Particulate Effects on Osteoblast Function," M.S. Thesis, Department of Chemical Engineering, Rice University, March 1997.
2. Anna C. Jen, "Effects of Mechanical Loading on Osteoblast Function Using a Three-Dimensional Cell/Polymer Construct," M.S. Thesis, Department of Chemical Engineering, Rice University, May 1997.
3. Albert K. Shung, "Synthesis and Characterization of an Injectable Copolymer Hydrogel for Cardiovascular Applications," M.S. Thesis, Department of Bioengineering, Rice University, June 2002.
4. Jeffrey E.-K. Chen, "Evaluation of Adhesive Properties of Poly(Propylene Fumarate) and Fabrication of Laminated Three-Dimensional Scaffolds for Bone Tissue Engineering," M.S. Thesis, Department of Chemical Engineering, Rice University, September 2002.
5. Andrea Haesslein, "Development of Ocular Drug Delivery Systems Using Biodegradable Polymers," M.S. Thesis, Department of Bioengineering, Rice University, April 2007.
6. Sheila A. Moore, "Synthesis and Characterization of Matrix Metalloproteinase Sensitive Hydrogels for Articular Cartilage Engineering," M.S. Thesis, Department of Bioengineering, Rice University, April 2007.

Current Theses Supervision

1. Sue Anne Chew, "Injectable Biodegradable Hydrogels for Multiple Growth Factor Delivery," Ph.D. Thesis, Department of Bioengineering, Rice University (expected completion May 2009).
2. Xuan Guo, "Fabrication of Tissue Engineering Hydrogel Scaffolds of Controlled Architecture," Ph.D. Thesis, Department of Chemical Engineering, Rice University (expected completion May 2009).

3. Jiehong Liao, "Cell and Growth Factor Delivery Using Injectable Biodegradable Hydrogels," Ph.D. Thesis, Department of Bioengineering, Rice University (expected completion May 2009).
4. Anita Saraf, "Development of Non-Viral Biodegradable Polymeric Carriers for Gene Delivery," Ph.D. Thesis, Department of Bioengineering, Rice University (expected completion May 2009).
5. Ana M. Martins, "Development of Biomimetic Biodegradable Scaffolds for Bone Tissue Engineering," Department of Polymer Engineering, University of Minho, Portugal (expected completion May 2009).
6. Leda Klouda, "Calcium-Binding Hydrogels for Guided Bone Regeneration," Ph.D. Thesis, Department of Bioengineering, Rice University (expected completion May 2010).
7. James D. Kretlow, "Injectable, *In Situ* Hardening Cellular Constructs for Bone Tissue Engineering," Ph.D. Thesis, Department of Bioengineering, Rice University (expected completion May 2010).
8. Richard A. Thibault, "Generation of Osteoinductive Extracellular Matrix Constructs with a Flow Perfusion Bioreactor," Ph.D. Thesis, Department of Bioengineering, Rice University (expected completion May 2011).
9. Emily L. Burdett, "Development of a 3-D Tissue Engineered Cancer Model for Testing Chemotherapeutics," Ph.D. Thesis, Department of Bioengineering, Rice University (expected completion May 2012).
10. Paschalia M. Mountziaris, "Bone Healing Enhancement by Modulation of Molecular Signaling," Ph.D. Thesis, Department of Bioengineering, Rice University (expected completion May 2012).

Teaching Experience

Rice University

BIOE 370 (U/N): "Biomaterials," Fall 2007 and 2008
BIOE 620/CENG 620 (G, N): "Tissue Engineering," Spring 1993, 1995, 1997, 1999, 2000, 2001, 2002, 2003, 2004, 2006, 2007, and 2008
BIOE 420/CENG 420 (U/G, N): "Biosystems Transport and Reaction Processes," Spring 1994, Fall 1995, 1996, 1997, 1998, 1999, 2000, 2001, 2002, 2004, 2005, and 2006
CENG 672 (G): "Applied Mathematics I," Fall 1992, 1993, 1994, 1995, 1996, and 1997
CENG 343 (U): "Chemical Engineering Lab," Fall 1993

University of Texas Health Science Center at Houston, Dental Branch

GS210082 (G): "Oral Biomaterials I," Summer 1994 and 1995

M.I.T.

10.362 (U): "Integrated Chemical Engineering," Spring 1991 (with Prof. R. Langer)

U=Undergraduate; G=Graduate; N=New Course Not Previously Given at Rice

Service at Rice University

1992	Organizer, Chemical Engineering Colloquium
1992-	Faculty Associate, Sid Richardson College
1992-2000	Graduate Recruiting Committee Member, Department of Chemical Engineering
1992-2000	Library Representative, Department of Chemical Engineering
1992	Trainer, NIH Minority High School Student Research Apprentice Program
1993-1994	Graduate Curriculum Committee Member, Bioengineering Program
1994	Organizing Committee Member, Biochemistry and Cell Biology Retreat
1994-1996	Organizer, Chemical Engineering Graduate Research Poster Contest
1994-2000	Steering Committee Member, NIH Biotechnology Training Program
1995-	Faculty Operating Committee Member, Medical Scientist Training Program, Baylor College of Medicine/Rice University
1996	Organizer, Chemical Engineering Colloquium
1996	Organizer, Chemical Engineering Graduate Research Symposium
1996-1997	Undergraduate Curriculum Committee Member, Department of Bioengineering
1998-2001	Graduate Recruiting Committee Member, Department of Bioengineering
1999	Faculty Search Committee Member, Department of Bioengineering
1999-2006	Undergraduate Admissions Committee Member, Rice University
2001	Organizer, Symposium Celebrating Keck Hall, the New Home of the Department of Bioengineering, and Honoring Professor J. David Hellums
2000-2001	Awards Committee Chair, Department of Bioengineering
2000-2001	Faculty Search Committee Chair, Department of Bioengineering
2001	Trainer, NSBRI High School Student Research Apprentice Program
2001-2006	Steering Committee Member, NSF IGERT Program
2002	Faculty Search Committee Member, Department of Bioengineering
2002-2005	Awards and Mentoring Committee Chair, Department of Bioengineering
2002-	Graduate Academic Affairs Committee Chair, Department of Bioengineering
2003-2004	Chair Search Committee Member, Department of Bioengineering
2004-2005	Dean of Engineering Search Committee Member, School of Engineering
2005-	Faculty Search Committee Member, Department of Bioengineering
2005-	Cain Project Faculty Advisory Committee Member, Rice University
2006-	Executive Committee Member, Medical Scientist Training Program, Baylor College of Medicine/Rice University

The PROMUS™ Everolimus Eluting Coronary Stent System
Instructions for Use

℞ ONLY

Table of Contents

1.0 PRODUCT DESCRIPTION

The PROMUS™ Everolimus-Eluting Coronary Stent System (PROMUS EECSS or PROMUS stent system) is a private label XIENCE™ V Everolimus Eluting Coronary Stent System (XIENCE V EECSS or XIENCE V stent system) manufactured by Abbott and distributed by Boston Scientific Corporation. The PROMUS V EECSS is a device/drug combination product consisting of either the MULTI-LINK VISION® Coronary Stent System or the MULTI-LINK MINI VISION® Coronary Stent System coated with a formulation containing everolimus, the active ingredient, embedded in a non-erodible polymer.

1.1 Device Component Description

The device component consists of the MULTI-LINK MINI VISION or MULTI-LINK VISION stent mounted onto the MULTI-LINK MINI VISION or MULTI-LINK VISION stent delivery system (SDS) respectively. The device component characteristics are summarized in Table 1-1.

Table 1-1: PROMUS Stent System Product Description

	PROMUS Rapid-Exchange (RX) EECSS	PROMUS Over-the-Wire (OTW) EECSS
Available Stent Lengths (mm)	8, 12, 15, 18, 23, 28	8, 12, 15, 18, 23, 28
Available Stent Diameters (mm)	2.5, 2.75, 3.0, 3.5, 4.0	2.5, 2.75, 3.0, 3.5, 4.0
Stent Material	A medical grade L-605 cobalt chromium (CoCr) alloy MULTI-LINK VISION or MULTI-LINK MINI VISION stent	
Drug Component	A conformal coating of a non-erodible polymer loaded with 100 µg/cm^2 of everolimus with a maximum nominal drug content of 181 µg on the large stent (4.0 x 28 mm)	
Delivery System Working Length	143 cm	143 cm
Delivery System Design	Single access port to inflation lumen. Guide wire exit notch is located 30 cm from tip. Designed for guide wires ≤ 0.014".	Sidearm adaptor provides access to balloon inflation/deflation lumen and guide wire lumen. Designed for guide wires ≤ 0.014".
Stent Delivery System Balloon	A compliant, tapered balloon, with two radiopaque markers located on the catheter shaft to indicate balloon positioning and expanded stent length.	
Balloon Inflation Pressure	Nominal inflation pressure: 8 atm (811 kPa) for 2.5 and 2.75 mm diameters; 9 atm (912 kPa) for 3.0, 3.5, and 4.0 mm diameters Rated Burst Pressure (RBP): 16 atm (1621 kPa) for all sizes	
Guiding Catheter Inner Diameter	≥ 5 F (0.056")	
Catheter Shaft Outer Diameter (nominal)	2.5–3.0 mm / 3.5–4.0 mm Distal: 0.032" / 0.035" Proximal: 0.026" / 0.026"	2.5 mm / 2.75 x 8 – 3.5 x 18 / 3.5 x 23 – 4.0 x 28 Distal: 0.032" / 0.034" / 0.036" Proximal: 0.042" / 0.042" / 0.042"

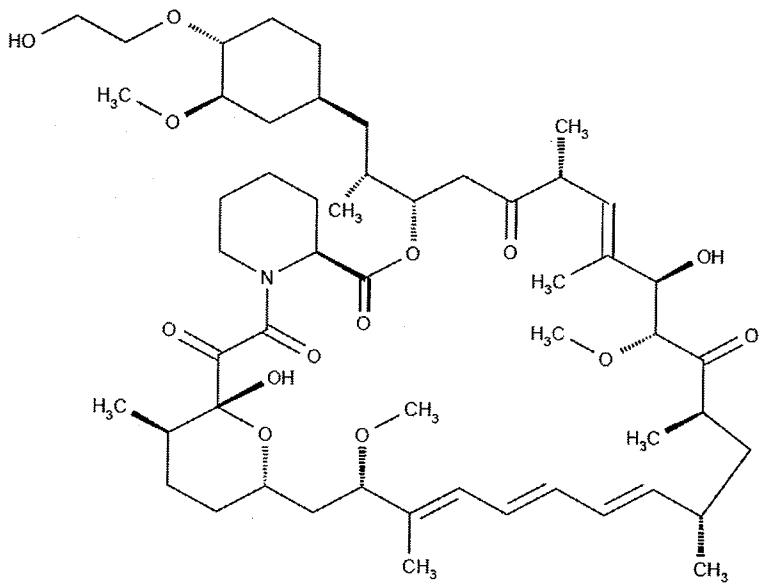
1.2 Drug Component Description

The PROMUS Everolimus- Eluting Coronary Stent (PROMUS stent) is coated with everolimus (active ingredient), embedded in a non-erodible polymer (inactive ingredient).

1.2.1 Everolimus

Everolimus is the active pharmaceutical ingredient in the PROMUS stent. It is a novel semi-synthetic macrolide immunosuppressant, synthesized by chemical modification of rapamycin (sirolimus). The everolimus chemical name is 40-O-(2-hydroxyethyl)-rapamycin and the chemical structure is shown in Figure 1-1 below.

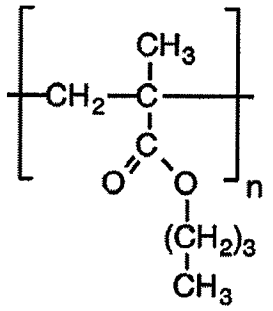
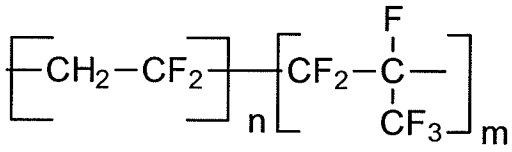
Figure 1-1: Everolimus Chemical Structure



1.2.2. Inactive Ingredients – Non-erodible Polymer

The PROMUS stent contains inactive ingredients including poly n-butyl methacrylate (PBMA), a polymer that adheres to the stent and drug coating, and PVDF-HFP, which is comprised of vinylidene fluoride and hexafluoropropylene monomers as the drug matrix layer containing everolimus. PBMA is a homopolymer with a molecular weight (Mw) of 264,000 to 376,000 dalton. PVDF-HFP is a non-erodible semi-crystalline random copolymer with a molecular weight (Mw) of 254,000 to 293,000 dalton. The drug matrix copolymer is mixed with everolimus (83%/17% w/w polymer/everolimus ratio) and applied to the entire PBMA coated stent surface. The drug load is 100 $\mu g/cm^2$ for all product sizes. No topcoat layer is used. The polymer chemical structures are shown in Figure 1-2 below.

Figure 1-2: Non-erodible Polymer Chemical Structures

PBMA	PVDF-HFP
	

1.2.3 Product Matrix and Everolimus Content

Table 1-3: PROMUS EECSS Product Matrix and Everolimus Content

Model Number (RX)	Model Number (OTW)	Nominal Expanded Stent Diameter (mm)	Nominal Unexpanded Stent Length (mm)	Nominal Everolimus Content (µg)
1009539-08B	1009545-08B	2.5	8	37
1009540-08B	1009546-08B	2.75	8	37
1009541-08B	1009547-08B	3.0	8	37
1009542-08B	1009548-08B	3.5	8	53
1009543-08B	1009549-08B	4.0	8	53
1009539-12B	1009545-12B	2.5	12	56
1009540-12B	1009546-12B	2.75	12	56
1009541-12B	1009547-12B	3.0	12	56
1009542-12B	1009548-12B	3.5	12	75
1009543-12B	1009549-12B	4.0	12	75
1009539-15B	1009545-15B	2.5	15	75
1009540-15B	1009546-15B	2.75	15	75
1009541-15B	1009547-15B	3.0	15	75
1009542-15B	1009548-15B	3.5	15	98
1009543-15B	1009549-15B	4.0	15	98
1009539-18B	1009545-18B	2.5	18	88
1009540-18B	1009546-18B	2.75	18	88
1009541-18B	1009547-18B	3.0	18	88
1009542-18B	1009548-18B	3.5	18	113
1009543-18B	1009549-18B	4.0	18	113
1009539-23B	1009545-23B	2.5	23	113
1009540-23B	1009546-23B	2.75	23	113
1009541-23B	1009547-23B	3.0	23	113
1009542-23B	1009548-23B	3.5	23	151
1009543-23B	1009549-23B	4.0	23	151
1009539-28B	1009545-28B	2.5	28	132
1009540-28B	1009546-28B	2.75	28	132
1009541-28B	1009547-28B	3.0	28	132
1009542-28B	1009548-28B	3.5	28	181
1009543-28B	1009549-28B	4.0	28	181

2.0 INDICATIONS

The PROMUS Everolimus-Eluting Coronary Stent System (PROMUS stent) is indicated for improving coronary luminal diameter in patients with symptomatic heart disease due to *de novo* native coronary artery lesions (length ≤ 28 mm) with reference vessel diameters of 2.5 mm to 4.25 mm.

3.0 CONTRAINDICATIONS

The PROMUS stent is contraindicated for use in patients:

- Who cannot receive antiplatelet and/or anti-coagulant therapy (see **Section 5.2 Pre- and Post-Procedure Antiplatelet Regimen** for more information)
- With lesions that prevent complete angioplasty balloon inflation or proper placement of the stent or stent delivery system
- With hypersensitivity or contraindication to everolimus or structurally-related compounds, cobalt, chromium, nickel, tungsten, acrylic, and fluoropolymers

4.0 WARNINGS

- Ensure that the inner package sterile barrier has not been opened or damaged prior to use.
- Judicious patient selection is necessary because device use has been associated with stent thrombosis, vascular complications, and/or bleeding events.
- This product should not be used in patients who are not likely to comply with the recommended antiplatelet therapy (see Section 5.2 for important information regarding antiplatelet therapy).

5.0 PRECAUTIONS

5.1 General Precautions

- Stent implantation should only be performed by physicians who have received appropriate training.
- Stent placement should be performed at hospitals where emergency coronary artery bypass graft surgery is accessible.
- Subsequent restenosis may require repeat dilatation of the arterial segment containing the stent. Long-term outcomes following repeat dilatation of the stent is presently unknown.
- Risks and benefits should be considered in patients with severe contrast agent allergies.
- Care should be taken to control the guiding catheter tip during stent delivery, deployment, and balloon withdrawal. Before withdrawing the stent delivery system, visually confirm complete balloon deflation by fluoroscopy to avoid guiding catheter movement into the vessel and subsequent arterial damage.
- Stent thrombosis is a low-frequency event that current drug-eluting stent (DES) clinical trials are not adequately powered to fully characterize. Stent thrombosis is frequently associated with myocardial infarction (MI) or death. Data from the SPIRIT family of trials have been prospectively evaluated and adjudicated using both the protocol definition of stent thrombosis and the definition developed by the Academic Research Consortium (ARC), and demonstrate specific patterns of stent thrombosis that vary depending on the definition used (see Section 8.2 Stent Thrombosis Definitions and Section 9.4 SPIRIT II and SPIRIT III Pooled Analysis, for more information). In the SPIRIT family of trials analyzed to date, the differences in the incidence of stent thrombosis observed with the stent, used in the SPIRIT clinical trials, compared to the TAXUS stent have not been associated with an increased risk of cardiac death, MI, or all-cause mortality. Additional data from longer-term follow-up in the SPIRIT family of trials and analyses of DES-related stent thrombosis are expected and should be considered in making treatment decisions as data become available.
- When DES are used outside the specified Indications for Use, patient outcomes may differ from the results observed in the SPIRIT family of trials.
- Compared to use within the specified Indications for Use, the use of DES in patients and lesions outside of the labeled indications, including more tortuous anatomy, may have an increased risk of adverse events, including stent thrombosis, stent embolization, MI, or death.

- Orally administered everolimus combined with cyclosporine is associated with increased serum cholesterol and triglycerides levels.

5.2 Pre- and Post-Procedure Antiplatelet Regimen

- In SPIRIT FIRST clinical trial, clopidogrel bisulfate or ticlopidine hydrochloride was administered pre-procedure and for a minimum of 3 months post-procedure (75 mg per day). In SPIRIT II and SPIRIT III clinical trials, clopidogrel bisulfate or ticlopidine hydrochloride was administered pre-procedure and for a minimum of 6 months post-procedure (75 mg per day). Aspirin was administered (a minimum of 75 mg per day) pre-procedure and continued for 1 to 5 years (depending on the study). Based on the case report forms from the SPIRIT II and III randomized clinical trials, approximately 92% of patients remained on dual antiplatelet therapy at 6 months and 62% at 1 year See Section 9.0 – Clinical Studies, for more specific information.
- The optimal duration of dual antiplatelet therapy, specifically clopidogrel, is unknown and DES thrombosis may still occur despite continued therapy. Data from several studies on sirolimus-eluting or paclitaxel-eluting stents suggest that a longer duration of clopidogrel than was recommended post-procedurally in DES pivotal trials may be beneficial. Current guidelines recommend that patients receive aspirin indefinitely and that clopidogrel therapy be extended to 12 months in patients at low risk of bleeding (ref: ACC/AHA/SCAI PCI Practice Guidelines[1,2]).
- It is very important that the patient is compliant with the post-procedural antiplatelet therapy recommendations. Early discontinuation of prescribed antiplatelet medication could result in a higher risk of thrombosis, MI, or death. Prior to percutaneous coronary intervention (PCI), if the patient is required to undergo a surgical or dental procedure that might require early discontinuation of antiplatelet therapy, the interventionalist and patient should carefully consider whether a DES and its associated recommended antiplatelet therapy is the appropriate PCI treatment of choice. Following PCI, should a surgical or dental procedure be recommended that requires suspension of antiplatelet therapy, the risks and benefits of the procedure should be weighed against the possible risks associated with early discontinuation of antiplatelet therapy. Patients who require early discontinuation of antiplatelet therapy (e.g., secondary to active bleeding) should be monitored carefully for cardiac events. At the discretion of the patient's treating physicians, the antiplatelet therapy should be restarted as soon as possible.

5.3 Multiple Stent Use

A patient's exposure to drug and polymer is proportional to the number and total length of implanted stents. In the SPIRIT II and III clinical trials, treatment was limited to 36 mm of total stent length in up to two lesions in different epicardial vessels. Use of more than two stents to treat lesions longer than 28 mm has not been evaluated and may increase patient complication risks. Studies evaluating the effects of higher drug doses have not been conducted.

Effects of multiple stenting using PROMUS stents combined with other drug-eluting stents are also unknown. When multiple drug-eluting stents are required, use only PROMUS stents in order to avoid potential interactions with other drug-eluting or coated stents.

[1] Smith et al. ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. JACC, 2006; 47: e1-121.
[2] King III et al. 2007 Focused Update of the ACC/AHA/SCAI 2005 Guideline Update for Percutaneous Coronary Intervention. JACC, 2008; 51:172-209.

In addition, only stents composed of similar materials should be implanted in consecutive stent to stent contact to avoid corrosion potential between unrelated materials. Although *in vitro* tests combining L-605 CoCr alloy with 316 L stainless steel did not increase corrosion potential, these studies have not been conducted *in vivo*.

5.4 Brachytherapy

PROMUS stent safety and effectiveness has not been evaluated in patients with prior target lesion or in-stent restenosis-related brachytherapy.

5.5 Use in Conjunction with Other Procedures

The safety and effectiveness of using mechanical atherectomy devices (directional atherectomy catheters, rotational atherectomy catheters) or laser angioplasty catheters in conjunction with PROMUS stent implantation have not been established.

5.6 Use in Special Populations

5.6.1 Pregnancy

Pregnancy Category C. See Section 6.5 – Drug Information, Pregnancy. The PROMUS stent has not been tested in pregnant women or in men intending to father children. Effects on the developing fetus have not been studied. Effective contraception should be initiated before implanting a PROMUS stent and continued for one year after implantation. While there is no contraindication, the risks and reproductive effects are unknown at this time.

5.6.2 Lactation

See Section 6.6 – Drug Information, Lactation. A decision should be made whether to discontinue nursing prior to stent implantation considering the importance of the stent to the mother.

5.6.3 Gender

No safety- or effectiveness-related gender differences were observed in the individual SPIRIT clinical trials.

5.6.4 Ethnicity

Insufficient SPIRIT clinical trial subject numbers prevent ethnicity-related analyses on safety and effectiveness.

5.6.5 Pediatric Use

Safety and effectiveness of the PROMUS stent in pediatric subjects have not been established.

5.6.6 Geriatric Use

SPIRIT clinical studies did not suggest that patients age 65 years and over differed with regard to safety and effectiveness compared to younger patients.

5.7 Lesion/Vessel Characteristics

Safety and effectiveness of the PROMUS stent have not been established for subject populations with the following clinical settings:

- Unresolved vessel thrombus at the lesion site
- Coronary artery reference vessel diameters < 2.5 mm or > 4.25 mm
- Lesion lengths > 28 mm
- Lesions located in saphenous vein grafts
- Lesions located in unprotected left main coronary artery, ostial lesions, chronic total occlusions, lesions located at a bifurcation
- Previously stented lesions
- Diffuse disease or poor flow (TIMI < 1) distal to the identified lesions
- Excessive tortuosity proximal to or within the lesion
- Recent acute myocardial infarction (AMI) or evidence of thrombus in the target vessel
- Moderate or severe lesion calcification
- Multivessel disease
- In-stent restenosis
- Patients with longer than 24 months follow-up.

5.8 Drug Interactions

See Section 6.3 – Drug Information, Interactions with Drugs or Other Substances.
Several drugs are known to affect everolimus metabolism, and other drug interactions may also occur. Everolimus is known to be a substrate for both cytochrome P4503A4 (CYP3A4) and P-glycoprotein. Everolimus absorption and subsequent elimination may be influenced by drugs that affect these pathways. Everolimus has also been shown to reduce the clearance of some prescription medications when administered orally along with cyclosporine (CsA). Formal drug interaction studies have not been performed with the PROMUS stent because of limited systemic exposure to everolimus eluted from the stent used in SPIRIT clinical trials (see Section 6.2 Pharmacokinetics). Therefore, due consideration should be given to the potential for both systemic and local drug interactions in the vessel wall when deciding to place the PROMUS stent in a patient taking a drug with known interaction with everolimus, or when deciding to initiate therapy with such a drug in a patient who has recently received a PROMUS Stent.

5.9 Immune Suppression Potential

Everolimus, the PROMUS stent active ingredient, is an immunosuppressive agent. Immune suppression was not observed in the SPIRIT clinical trials. However, for patients who receive several PROMUS stents simultaneously, it may be possible for everolimus systemic concentrations to approach immunosuppressive levels temporarily, especially in patients who also have hepatic insufficiency or who are taking drugs that inhibit CYP3A4 or P-glycoprotein. Therefore, consideration should be given to patients taking other immunosuppressive agents or who are at risk for immune suppression.

5.10 Lipid Elevation Potential

Oral everolimus use in renal transplant patients was associated with increased serum cholesterol and triglycerides that in some cases required treatment. The effect was seen with both low and high dose prolonged oral therapy in a dose related manner. When used according to the indications for use, exposure to systemic everolimus concentrations from the PROMUS stent are expected to be significantly lower than concentrations usually obtained in transplant patients. Increased serum cholesterol and triglycerides were not observed in the SPIRIT family of clinical trials.

5.11 Magnetic Resonance Imaging (MRI)

Non-clinical testing has demonstrated that the PROMUS stent, in single and in overlapped configurations up to 68 mm in length, is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5 or 3 Tesla
- Spatial gradient field of 720 Gauss/cm or less
- Maximum whole-body-averaged specific absorption rate (SAR) of 2.0 W/kg (normal operating mode) for 15 minutes of scanning or less

The PROMUS stent should not migrate in this MRI environment. Non-clinical testing at field strengths greater than 3 Tesla has not been performed to evaluate stent migration or heating. MRI at 1.5 or 3 Tesla may be performed immediately following the implantation of the PROMUS stent.

Stent heating was derived by relating the measured non-clinical, *in vitro* temperature rises in a GE Excite 3 Tesla scanner and in a GE 1.5 Tesla coil to the local specific absorption rates (SARs) in a digitized human heart model. The maximum whole body averaged SAR was determined by validated calculation. At overlapped lengths up to 68 mm, the PROMUS stent produced a non-clinical maximum local temperature rise of 3°C at a maximum whole body averaged SAR of 2.0 W/kg (normal operating mode) for 15 minutes. These calculations do not take into consideration the cooling effects of blood flow.

The effects of MRI on overlapped stents greater than 68 mm in length or stents with fractured struts are unknown.

As demonstrated in non-clinical testing, an image artifact can be present when scanning the PROMUS stent. MR image quality may be compromised if the area of interest is in the exact same area, or relatively close to, the position of the PROMUS stent. Therefore, it may be necessary to optimize the MR imaging parameters for the presence of PROMUS stents.

5.12 Stent Handling

- **Each stent is for single use only.** Do not resterilize or reuse this device. Note the "use by" (expiration) date on the product label.
- **The foil pouch is not a sterile barrier.** The inner header bag (pouch) within the foil pouch is the sterile barrier. **Only the contents of the inner pouch should be considered sterile. The outside surface of the inner pouch is NOT sterile.**
- **Do not remove the stent from the delivery system.** Removal may damage the stent and/or lead to stent embolization. These components are intended to perform together as a system.
- The delivery system should not be used in conjunction with other stents.
- Special care must be taken not to handle or disrupt the stent on the balloon especially during delivery system removal from packaging, placement over the guide wire and advancement through the rotating hemostatic valve adapter and guiding catheter hub.
- **Do not manipulate, touch, or handle the stent** with your fingers, which may cause coating damage, contamination, or stent dislodgement from the delivery balloon.
- Use only the appropriate balloon inflation media (see Section 13.3.3 – Operator's Instructions, Delivery System Preparation). Do not use air or any gaseous medium to inflate the balloon as this may cause uneven expansion and difficulty in stent deployment.

5.13 Stent Placement

5.13.1 Stent Preparation

- **Do not prepare or pre-inflate the delivery system prior to stent deployment other than as directed.** Use the balloon purging technique described in Section 13.3.3 – Operator's Instructions, Delivery System Preparation.
- **Do not induce negative pressure on the delivery system prior to placing the stent across the lesion.** This may cause dislodgement of the stent from the balloon.
- Use guiding catheters which have lumen sizes that are suitable to accommodate the stent delivery system (see Section 1.1 – Product Description, Device Component Description).

5.13.2 Stent Implantation

- The vessel should be pre-dilated with an appropriate sized balloon. Failure to do so may increase the difficulty of stent placement and cause procedural complications.
- Do not expand the stent if it is not properly positioned in the vessel (see Section 5.14 – Precautions, Stent System Removal).
- Implanting a stent may lead to vessel dissection and acute closure requiring additional intervention (CABG, further dilatation, placement of additional stents, or other).
- Although the safety and effectiveness of treating more than one vessel per coronary artery with PROMUS stents has not been established, if this is performed, place the stent in the distal lesion before the proximal lesion in order to minimize dislodgement risk incurred by traversing through deployed stents.
- Stent placement may compromise side branch patency.
- **Do not exceed Rated Burst Pressure (RBP) as indicated on product label.** See Table 14-1, Typical PROMUS EECSS Compliance. Balloon pressures should be monitored during inflation. Applying pressures higher than specified on the product label may result in a

ruptured balloon with possible arterial damage and dissection. The stent inner diameter should approximate 1.1 times the reference diameter of the vessel.

- An unexpanded stent may be retracted into the guiding catheter one time only. An unexpanded stent should not be reintroduced into the artery once it has been pulled back into the guiding catheter. Subsequent movement in and out through the distal end of the guiding catheter should not be performed as the stent may be damaged when retracting the undeployed stent back into the guiding catheter.
- Should **any resistance** be felt **at any time** during coronary stent system withdrawal, the stent delivery system and guiding catheter should be **removed as a single unit** (see Section 5.14 – Precautions, Stent System Removal).
- Stent retrieval methods (i.e., using additional wires, snares, and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include bleeding, hematoma, or pseudoaneurysm.
- Although the stent delivery system balloon is strong enough to expand the stent without rupture, a circumferential balloon tear distal to the stent and prior to complete stent expansion, could cause the balloon to become tethered to the stent, requiring surgical removal. In case of balloon rupture, it should be withdrawn and, if necessary, a new dilatation catheter exchanged over the guide wire to complete the expansion of the stent.
- Ensure the stented area covers the entire lesion/dissection site and that no gaps exist between stents.

5.14 Stent System Removal

Should **any resistance** be felt **at any time** during either lesion access or removing the delivery system post-stent implantation, the stent delivery system and the guiding catheter should be **removed as a single unit.**

When removing the delivery system and guiding catheter as a single unit, the following steps should be executed under direct visualization using fluoroscopy:

- Confirm complete balloon deflation. If unusual resistance is felt during stent delivery system withdrawal, pay particular attention to the guiding catheter position. In some cases it may be necessary to slightly retract the guiding catheter in order to prevent unplanned guiding catheter movement and subsequent vessel damage. In cases where unplanned guiding catheter movement has occurred, a coronary tree angiographic assessment should be undertaken to ensure that there is no damage to the coronary vasculature.
- DO NOT retract the delivery system into the guiding catheter.
- Position the proximal balloon marker just distal to guiding catheter tip.
- Advance the guide wire into the coronary anatomy as far distally as safely possible.
- Tighten the rotating hemostatic valve to secure the delivery system to the guiding catheter, and remove the guiding catheter and delivery system as a **single unit.**

Failure to follow these steps and/or applying excessive force to the delivery system can potentially result in loss or damage to the stent and/or delivery system components.

If it is necessary to retain guide wire position for subsequent artery/lesion access, leave the guide wire in place and remove all other system components.

Stent retrieval methods (i.e., additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications may include, but are not limited to, bleeding, hematoma, or pseudoaneurysm.

5.15 Post-Procedure

- When **crossing a newly deployed stent** with an intravascular ultrasound (IVUS) catheter, a coronary guide wire, a balloon catheter or delivery system, exercise care to avoid disrupting the stent placement, apposition, geometry, and/or coating.
- Antiplatelet therapy should be administered post-procedure (see Section 5.2 Pre- and Post-Procedure Antiplatelet Regimen and Section 9.0 Clinical Studies). Patients who require early discontinuation of antiplatelet therapy (e.g., secondary to active bleeding) should be monitored carefully for cardiac events. At the discretion of the patient's treating physician, the antiplatelet therapy should be restarted as soon as possible.
- If the patient requires imaging, see Section 5.11 – Precautions, Magnetic Resonance Imaging (MRI).

6.0 DRUG INFORMATION

6.1 Mechanism of Action

The mechanism by which the PROMUS Stent inhibits neointimal growth as seen in pre-clinical and clinical studies has not been established. At the cellular level, everolimus inhibits growth factor-stimulated cell proliferation. At the molecular level, everolimus forms a complex with the cytoplasmic protein FKBP-12 (FK 506 Binding Protein). This complex binds to and interferes with FRAP (FKBP-12 Rapamycin Associated Protein), also known as mTOR (mammalian Target Of Rapamycin), leading to inhibition of cell metabolism, growth and proliferation by arresting the cell cycle at the late G1 stage.

6.2 Pharmacokinetics of the XIENCE V Everolimus Eluting Coronary Stent

The PROMUS Everolimus-Eluting Coronary Stent System is a private label XIENCE V Everolimus Eluting Coronary Stent System manufactured by Abbott and distributed by Boston Scientific Corporation. Everolimus pharmacokinetics (PK) when eluted from the XIENCE V stent used in the SPIRIT clinical trials post-implantation has been evaluated in three different substudies in three different geographies. The SPIRIT III clinical trial design includes a pharmacokinetic substudy in the US randomized arm and a pharmacokinetic substudy in the Japanese non-randomized arm. The third PK substudy was conducted as part of the SPIRIT II clinical trial at sites in Europe, India, and New Zealand. Whole blood everolimus PK parameters determined from subjects receiving the XIENCE V stent are provided in Table 6-1.